THE BRITISH JOURNAL
OF
DERMATOLOGY
JUNE 1958

THE RETENTION OF ARSENIC IN THE LATE CUTANEOUS COMPLICATIONS OF ITS ADMINISTRATION.

A. SCOTT, M.D.

Department of Dermatology, St. Bartholomew's Hospltal, London.

DESPITE Osborne's (1925) original work to demonstrate the affinity of the epidermis for inorganic pentavalent arsenic, there is still considerable doubt as to the mechanism by which intake of arsenic effects the skin changes—keratoses and epitheliomata—whose subsequent development are attributed to it. This is largely due to the doubtful reliability of the methods used for arsenic estimations in the skin. The obvious limitations in the quantity of skin available preclude the use of the more usual methods of chemical measurement. The present paper is presented in order to outline a method of determination of the arsenical content in the skin, which appears to be acceptable in accuracy and comparative ease of use ; and on the basis of the results obtained to determine whether arsenic, given many years before, has been retained to any degree in the late manifestations of its administration.

METHOD.

1. *Patients.*—Fourteen patients with a history of arsenic intake (usually in the form of potassium arsenite for the treatment of psoriasis, epilepsy, or anaemia) were examined (Table I). In all cases but two, the medication had been taken regularly over a period of at least 10 years, but had been stopped for at least 4 years at the time of the test. The exceptions included one patient whose treatment had occupied only 7 years, and a second patient, on whom two estimations were done, who had had Fowler's solution as treatment for dermatitis herpetiformis for one month, four weeks prior to her first test.

Nine epitheliomata were analysed, 3 keratoses, and 4 biopsies of apparently normal skin, originating from the back (3), abdomen (1), chest (2), arm (4) and leg (5).

TABLE I.—*Summary of Arsenic Administration to the Tested Patients.*

Name.	Sex.	Present age (years).	Duration of arsenic therapy (years).	Time lapse since therapy (years).	Post-therapeutic complications.
C. G—	M.	76	22	9	Multiple superficial epitheliomata.
H. P—	,,	75	20	20	,, ,, ,,
M. H—	F.	65	35	6	,, ,, ,,
H. M—	,,	56	12	12	,, ,, ,,
G. I—	M.	69	7	30	,, ,, ,,
G. P—	,,	47	24	11	,, ,, ,,
B. T—	F.	75	30	25	,, ,, ,,
J. W—	,,	57	25	4	Multiple superficial epitheliomata, with keratoses and cirrhosis.
W. J—	,,	58	15	10	Multiple superficial epitheliomata.
E. B—	,,	64	22	16	Multiple superficial epitheliomata, with keratoses and cirrhosis.
W. M—	M.	50	30	8	Multiple superficial epitheliomata.
E. B—	F.	59	35	9	,, ,, ,,
G. R—	M.	54	30	10	,, ,, ,,
R. G—	,,	62	24	25	,, ,, ,,
M. C—	F.	61	$\frac{1}{12}$	$\frac{4}{52}$	*Nil.*

Two epitheliomata from the skin of patients working over a long period in contact with arsenical sprays were also tested, as well as normal skin from one of those patients.

None of the group of patients who had had arsenic gave any historical evidence of other arsenical dermatoses or arsenical toxic reactions.

The control group consisted of 6 patients ; 3 had superficial epitheliomata (two were post-irradiation and one familial) and no history of arsenic ingestion, and 3 patients with normal skin and no history of intake of this element.

2. Biopsies were of average size 1·0 × 0·5 cm., and their wet weight was obtained immediately after excision.

3. The tissue was placed in a plastic container, and exposed to irradiation in an atomic pile for about 24 hours.*

4. The specimen was next submitted to chemical separation of its arsenic content (now radioactive) using Marsh's method, and the material collected on filter paper (Bamford, 1940). The irradiated specimen was digested with sulphuric and nitric acids. The digest was then treated with dilute sulphuric acid, stannous chloride, ferrous sulphate and zinc in a modified Gutzeit apparatus, and the liberated arsine trapped by a disc of filter paper impregnated with silver nitrate, and clamped between two 10 mm. Pyrex flat flanges.

5. A Geiger counter with a thin window GM tube was used to measure the radioactivity of each specimen.

* Irradiation carried out at the Radioisotopes Division, Irradiation Unit, Amersham, Bucks.

6. With each set of samples submitted for irradiation, a standard tube containing a weighed quantity of arsenic was also supplied. A measure of the radioactivity in this standard then permitted us to convert the net counts obtained with the various samples into corresponding weights of contained arsenic. Under the conditions of analysis no radioactive material other than arsenic would be measured, and by using an identically treated standard the recovery would be practically theoretical.

Results.

The method outlined proved a satisfactory means of measuring minute quantities of arsenic even in small specimens (100 mg.) of skin, provided a standard sample of arsenic was submitted simultaneously for irradiation with each group of specimens. The results are summarized in Table II.

Table II.—*The Arsenic Content of Skin Samples.*

Name.	Diagnosis.	Wet weight (g.).	Net count (per min.).	Count/g.	Arsenic content (mg./g.).
History of Arsenic Intake.					
C. G—	Keratosis	0·20	575	2,875	6·9
W. J—	,,	0·15	51	340	0·8
E. B—	,,	0·40	236	840	2·3
H. P—	Epithelioma	0·20	181	905	1·8
M. H—	,,	0·15	75	500	1·0
H. M—	,,	0·15	258	1,720	3·6
G. I—	,,	0·15	152	1,013	2·0
G. P—	,,	0·25	254	1,016	2·0
B. T—	,,	1·39	1,522	1,091	2·2
J. W—	,,	0·15	71	573	1·0
E. B—	,,	0·65	1,355	2,085	3·8
B. T—	,,	0·23	965	4,288	8·9
W. M—	Normal skin	0·15	55	367	0·8
M. H—	,,	0·18	184	1,022	2·0
E. B—	,,	0·28	243	868	1·8
M. C—*	,, (1)	0·10	2,192	21,920	40·0
	,, (2)	0·10	34	340	1·0
External Contact with Arsenic.					
G. R—	Normal skin	1·51	891	592	1·9
	Epithelioma	1·40	3,884	2,773	5·7
R. G—	,,	1·80	6,275	3,486	7·2
No History of Arsenic Intake.					
W. P—	Post-irradiation basal-cell epithelioma (chest)	0·40	1,624	4,060	0·7
E. M—	Basal-cell epithelioma (familial) (abdomen)	0·73	208	271	0·4
H. H—	Post-irradiation basal-cell epithelioma (back)	0·20	1,024	5,120	1·0
P. R—	Normal skin (arm)	0·40	104	260	0·5
M. E—	,, (leg)	0·24	52	215	0·4
K. G—	,, (back)	0·40	287	718	0·7

* Patient with recent history of arsenic intake.

Samples from patients with normal skin and no history of arsenical intake contained between 0·4 and 1·0 micrograms of that element per gram of wet weight tissue. A similar range of values was obtained in tests of those patients with no previous arsenical therapy who had developed superficial epitheliomata from other causes.

The arsenic content of the nine epitheliomata removed from arsenic-treated patients was over 1·8 mcg./g. tissue in 7 of the 9 cases ; the remaining two gave values of 1·0 mcg./g. Of the 3 keratoses analyzed, 2 had values over 2·0 mcg./g. Three of the four biopsies with the highest content of arsenic were hyperkeratotic.

The apparently normal skin of the patients with a history of arsenic intake also contained an amount of arsenic greater than normal—in two of the three tested, 1·8 and 2·0 mcg./g.

The one patient who had received Fowler's solution for 1 month 4 weeks prior to her first test gave the highest value for skin arsenic content—40·0 mcg./g. ; however, it is interesting that in her second test, carried out 7 months later, the content of arsenic had fallen to 1·0 mcg./g.—within the recognized normal range. Both biopsies were done on normal skin.

Both patients who had been exposed to external contact with arsenic over a period of at least 20 years were found to have a high content of arsenic (5·7 and 7·2 mcg./g.) despite a time lapse of 10 and 25 years respectively since their last exposure. The one test of normal skin carried out in one of them also showed an elevated arsenic level.

Discussion.

Until recently the smallness of pieces of skin available for analysis has limited the accuracy of methods for the chemical estimation of arsenic in that tissue. By inducing radioactivity of the arsenic, this problem can be circumvented, provided that standard weights of arsenic are irradiated at the same time. Since all the other elements found in skin have a comparatively low specific activity and long half-life the radioactivity detected by this method is attributable solely to its arsenic content. The applicability of this method of estimation is limited to tissues which do not contain elements closely resembling arsenic in their radioactive isotopes.

The range of values determined for the content of arsenic in normal skin (0·4–1·0 mcg./g.) is in agreement with figures generally accepted by toxicologists.

The results outlined in Table II show that patients who have developed superficial epitheliomata as a result of the ingestion of a pentavalent form of arsenic tend to retain in their skin quantities of arsenic greater than the

normally expected amounts. These higher levels remain in the tissue over a long period—in some cases more than 30 years.

The quantity of arsenic retained in the skin bears no precise relationship to the duration of intake of arsenic, nor to the time lapse which has ensued between cessation of this form of therapy and the performance of the test. This suggests that there is an individual variation in the person's ability to handle and dispose of arsenic in the body.

Such a suggestion is supported by our observation in the one normal patient who had recently received arsenic. Although her initial levels of skin arsenic, 4 weeks after therapy had ceased, were high a second test done 7 months later showed that it had fallen to normal.

Finally, the comparative frequency with which arsenic-containing tonics were administered up to the 1930's suggests that there is a predisposition in some persons towards abnormal handling of arsenic in the body, since the incidence of these late complications is relatively low. This observation is compatible with the suggestion put forward by Montgomery and Waisman (1941) that arsenic acts as an activator of pre-existent latent foci of malignancy in susceptible individuals.

In our group of patients who had had arsenic, the content of this element was greater in those sites in which superficial epitheliomata had developed than in the rest of their skin. Levels were particularly high where hyperkeratosis was pronounced. This suggests that arsenic is bound in the keratin moiety.

In the cases exposed to external contact with arsenic, the concentration of the element in the epitheliomata was even greater than in those lesions which followed the ingestion of arsenic. This also suggests that these hyperkeratotic epitheliomata retained arsenic readily.

On the basis of these findings it may be proposed that, in a person with a history of arsenical therapy and who has a persistently high skin content of that element, the administration of BAL should be considered, to facilitate the elimination of residual arsenic and thereby reduce the chances of the development of malignant skin changes.

Summary.

1. The properties of irradiated arsenic may be used to assay that substance in small amounts of tissue.

2. The normal levels of arsenic in human skin are consistently below 1·0 mcg./g.

3. Patients who have been exposed to arsenic either through its ingestion or by external contact, and who have later developed keratoses and epitheliomata tend to have a higher than normal content of arsenic, not only in the actual lesion, but also in their normal skin.

4. There is an individual variation in the ability of persons to eliminate arsenic.

I should like to thank Dr. R. M. B. MacKenna and Dr. P. F. Borrie who suggested this investigation and criticized the work, and particularly Dr. V. R. Wheatley, formerly of the Biochemistry Department, for the performance of the chemical separations. The counting of radioactivity was done through the courtesy of Prof. J. Rotblat.

Bibliography.

Bamford, F. (1940) Marsh-Berzelius Test. In *Poisons. Their Isolation and Identification.* London : J. & A. Churchill Ltd.

Montgomery, H. and Waisman, M. (1941) *J. invest. Derm.*, **4**, 365.

Osborne, E. D. (1925) *Arch. Derm. Syph., Chicago,* **12**, 773.

A CASE OF FATAL METASTASIZING " ERYTHROPLASIA ".

MARY WITHAM, MAURICE GARRETTS, ARNOLD LEVINE AND ARTHUR JARRETT.

Dermatological Department, University College Hospital, London.

THE clinical appearance of erythroplasia described by Queyrat in 1911 is well known. All that is known of the histology, however, apparently based on that of his first case, is that it was a " parakeratotic lesion with epitheliomatous transformation ". Erythroplasia has subsequently been regarded as precancerous. Darier identified it with the condition which he had described in 1893 with Fournier under the name *épithéliome papillaire nu*. According to him, the surface is brilliant red and velvety. Sooner or later it develops into an invasive prickle-cell epithelioma. He mentions that these lesions are sometimes found on non-mucocutaneous parts of the skin, side by side with typical Bowen's disease.

Zoon (1950; 1952*a*, *b*) observed cases of erythroplasia characterized histologically by a plasma-cell infiltrate beneath a villous epidermis. He called this balanoposthitis chronica circumscripta plasmacellularis, regarded it as benign, and so differentiated it from Queyrat's erythroplasia. Garnier (1957) believes that the plasma-cell erythroplasia of Zoon is always benign.

The case reported here is thought to provide a link between the erythroplasia of Queyrat, the plasma-cell type of Zoon, and a sweat-duct carcinoma.

CASE REPORT.

This man was born in 1891. He suffered from epilepsy and had been treated with a bromide mixture, possibly containing liquor arsenicalis.

Skin lesions appeared in 1950. The patient first came to hospital in May 1953 when the first biopsy was taken from an erythematous discoid plaque 4 cm. in diameter on the left loin. He failed to attend for the next two years.

He was first seen by the present writers in July 1955 and was then found to have a bright red velvety oval plaque 9 cm. by 6 cm. on the left loin (Fig. 1). The area was granular, oozed serum, and bled when touched. It was very sharply defined, had a very thin but just perceptible rolled edge, and was painful. This clinical picture conformed closely to that of erythroplasia as described by Darier (Queyrat called the surface " smooth and glazed ").

He also had psoriasiform patches varying in size from 1 cm. to 6 cm. in diameter, scattered over the trunk. These were of a dull, brick red colour, with large adherent wafery scales. They proved histologically to be Bowen's disease, and yielded to CO_2 snow.

His serum Wassermann and Kahn reactions were negative, and his plasma bromide was 12·5 mg./100 ml.

At this time a second biopsy was made of the granular plaque. The surface was villous and covered by a layer of epithelium only one or two cells thick. Immediately beneath this was a dense infiltrate consisting mainly of plasma cells, with some mast

cells (Fig. 2). No changes suggestive of epithelioma were seen. This histopathology conformed to that of erythroplasia of the Zoon type. Its association with Bowen patches elsewhere on his skin aroused the strong suspicion that at some time it would reveal itself as epitheliomatous.

A third biopsy 3 weeks later from the opposite edge of the plaque showed a similar plasma-cell infiltrate, somewhat less dense ; but the epidermis showed irregularity of arrangement with some large cells possessing hyperchromatic nuclei, and some dyskeratotic cells of the type associated with Bowen's disease (Fig. 3).

At this stage, in October 1955, he was shown at the Dermatological Section of the Royal Society of Medicine (Garretts, 1956).

Treatment of the granular plaque with carbon dioxide snow resulted in gradual healing from the edge. The medial third (not yet treated) remained unchanged until April 1956 when a nodule about 1 cm. across appeared, and the whole lesion became hard to palpation. There were two small hard outlying nodules, connected to the main area by an indurated bar of tissue. A fourth biopsy taken from the nodule within the main plaque showed a neoplasm with the configuration of a basal-cell epithelioma, but many of the cells had much more cytoplasm than is usual for a basal cell. There were numerous mitoses, and considerable variation in the degree of cytoplasmic basophilia, and of size and shape of nuclei. These cells therefore did not conform to the usual appearance of either basal or squamous epidermal cells. There was a marked dermal infiltrate, and, as in the previous biopsies, this was mainly of plasma cells. The adjoining epidermis showed changes similar to those seen in Fig. 3. A fifth biopsy, taken from one of the outlying nodules, revealed a secondary carcinoma of the skin, with cords of cells having hyperchromatic nuclei and some multinucleated cells squeezing between the collagen bundles.

Extensive investigation failed to reveal any primary growth other than the granular plaque.

The granular plaque was thereupon treated with x-rays (5000 r, HVL 0·4 mm. Cu) given in divided daily doses over a period of two weeks. This resulted in some flattening of the surface but no decrease in the induration. Soon after this the tumour spread rapidly into the groins as cancer *en cuirasse*. Three weeks before death he developed a right pleural effusion, the fluid containing cells highly suggestive of carcinoma cells, and about this time lymph gland involvement produced massive oedema of both legs. His condition then rapidly deteriorated and he died on 13 : ix : 56.

Post-mortem Examination.

There was oedema of the left leg continuous above with a carcinoma *en cuirasse* which involved the upper thigh, scrotum, and approximately the left half of the abdomen and flank ; here the skin was nodular, ulcerated, thickened and indurated.

Heart.—Coronary artery atheroma.

Lungs.—Bilateral pleural effusions of 600 ml. were present with easily separated posterior pleural adhesions. The visceral pleurae of both lungs were coated with irregular greyish-white thin plaques, and a secondary deposit 3 mm. in diameter was found in the periphery of the right upper lobe. There was partial collapse of both lower lobes and the bronchi contained mucopus. No primary tumour was found, and paratracheal and hilar glands were either hard or necrotic.

Alimentary canal.—The oesophagus was normal. The stomach contained numerous ulcers, up to 2 cm. in diameter, scattered over its surface. The ulcer edges were raised and firm but not indurated, and no local hyperaemia was seen. The small and large intestines were normal.

Liver.—Average size and normal colour and consistency. A few scattered secondary deposits, none larger than 1 cm. in diameter. The bile ducts, portal vein, gall bladder and pancreas were normal.

Spleen.—Normal.

FIG. 1.

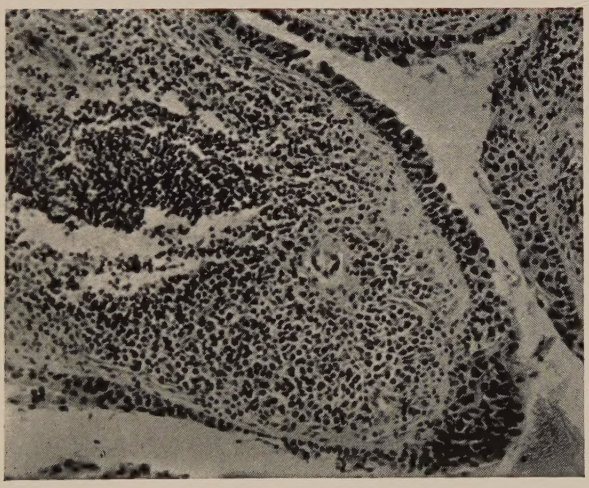

FIG. 2.—H. and E. × 150.

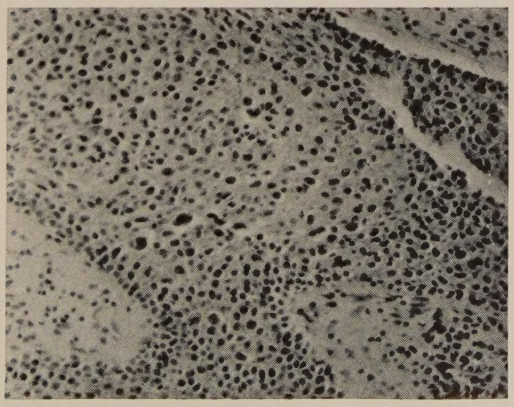

FIG. 3.—H. and E. × 100.

Kidneys.—A ureteric stricture 6 cm. above the right ureteric orifice was due to secondary deposits in the pelvis. Above the stricture the right ureter was dilated. The para-aortic glands were enlarged and white. The bladder and prostate were normal, but the testes were atrophied.

Ductless glands.—The pituitary was normal. There were bilateral multiple small secondaries in the adrenals. The thyroid showed a hard white infiltration of the left lower pole with a nodule in the right lobe.

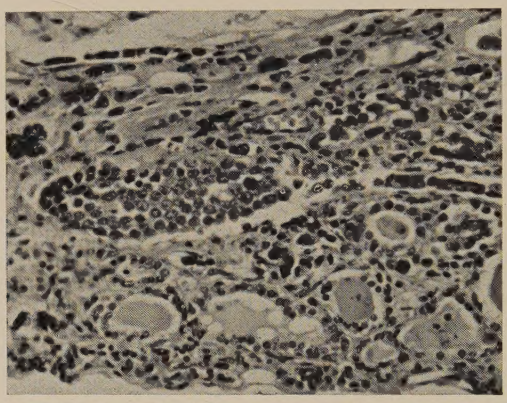

FIG. 4.—Secondary deposit in thyroid. There are two cell types : those with small hyperchromatic nuclei, and others with larger pale nuclei. H. and E. × 200.

FIG. 5.—Secondary deposit in stomach. There is a cystic area in the stomach wall with papilliferous ingrowths. H. and E. × 125.

The necropsy failed to reveal any primary tumour other than the skin carcinoma. Representative portions of several organs were taken for histology. Secondary growth was found infiltrating the liver, thyroid, stomach, lungs, lymph glands and skin.

The thyroid showed secondary deposits containing two distinct cell types (Fig. 4). Those in the stomach had papillary outgrowths into cystic duct formations (Fig. 5). The secondaries in the lungs and lymph glands were more anaplastic, consisting of deeply basophilic cells with pyknotic nuclei. The skin secondaries showed rudimentary acinar arrangement and resembled secondaries from a breast cancer.

Discussion.

This patient's granular plaque showed the histological changes, in one part, of Zoon's plasma-cell erythroplasia ; in another part, those of Bowen's disease. The plaque eventually became frankly malignant with local spread and metastases to internal organs.

Metastases have only rarely been described from intra-epidermal carcinomata, and these usually show the histology of squamous-cell epithelioma. Kuznitsky and Jacoby (1938) described a case of Bowen's disease with metastases showing " mixed epithelial and glandular elements ". Darier (1920), however, stated that the true histological picture of Bowen's disease must be seen in the metastases in order to make the diagnosis. Savatard (1935), besides suggesting that Bowen's disease, Paget's disease, and Queyrat's erythroplasia are all different forms of intra-epidermal carcinoma, stated that Bowen's disease is occasionally associated with a sweat-duct or gland carcinoma. Thus he correlated Bowen's disease with Paget's disease of the nipple, which may be associated with carcinoma of the mammary ducts. Civatte (1928) reported a case of sweat-gland carcinoma associated with Paget's disease of the axilla; presumably the carcinoma arose from an apocrine gland. Grzybowski (1933) also described sweat-duct and gland hyperplasia with early malignant change in association with intra-epidermal carcinomata.

Dockerty and Pratt (1952) described four cases of extramammary Paget's disease. They considered that this disorder was always preceded by an underlying apocrine carcinoma, and that the cells invaded the epidermis. This view is in agreement with that of Weiner (1937).

Recently Smith and Coburn (1956) have described a range of tumours under the term Hidroacanthoma Simplex. In one tumour there were histological changes of an intra-epidermal carcinoma. Part of this tumour, however, showed invasive changes with relatively narrow columns of cells of adenocarcinomatous type lying in a fibrocellular stroma.

The secondary deposits in the skin of our case were not histologically typical of squamous epithelioma. The cords of cells invading the tissue, and the rudimentary formation of acini could, however, be explained if a sweat-gland or duct carcinoma was responsible.

Metastases in the thyroid gland are rare. The metastatic deposit in the adenomatous thyroid could have occurred whether the primary growth was in the skin or one of the viscera, as it is known that a thyroid with an abnormality, usually a goitre, is predisposed to metastatic growths.

Another possible interpretation must be considered. This might be a case of microscopic primary visceral carcinoma which had metastasized to the skin and elsewhere. Were this so, it must be attributed to coincidence that it metastasized to an area of skin that was the site of a peculiar plaque already

suspected of being precancerous in a man with known precancerous patches on other parts of his skin. Moreover, at death, the skin cancer was of vastly greater extent than any of the visceral growths.

The patient had possibly ingested arsenic for many years, and this would make him prone to develop primary skin carcinoma. (Skin sections examined by the Castel method (1936) revealed no arsenic in the tissues, and spectroscopic analysis of one of the intra-epidermal carcinomata revealed less than 2 parts per million of arsenic.) It is not generally accepted that arsenic predisposes to the development of primary visceral cancers.

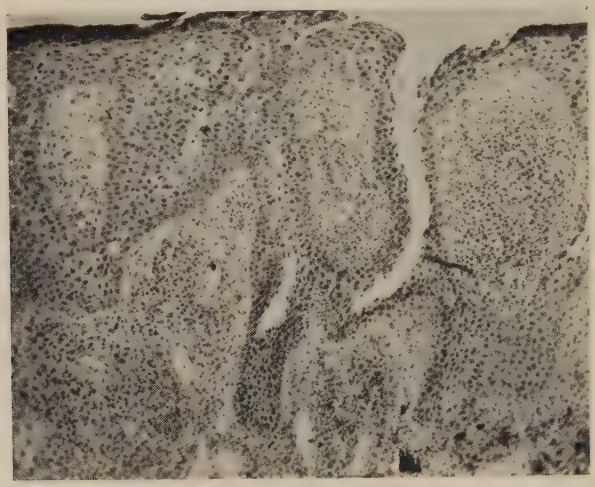

FIG. 6.—First biopsy from plaque taken $3\frac{1}{2}$ years before death. There is a dense plasma-cell infiltrate, Bowenoid changes in the epidermis, and evidence of sweat-duct proliferation. H. and E. × 100.

On re-examination of the biopsies taken from this patient, evidence was found of sweat-duct proliferation even in the earliest biopsy taken $3\frac{1}{2}$ years before death (Fig. 6). In subsequent biopsies this duct proliferation became more obvious and the plasma-cell infiltrate more pronounced.

In the second biopsy specimen there were changes distinctly resembling those seen in naevus syringadenomatosus papilliferus (Werther). Numerous glandular ducts ramified through massive plasma-cell infiltrates ; these ducts were lined on their outer aspect by small cuboidal cells of the myoepithelial type. The inner layer of columnar cells were in a state of great activity with numerous mitotic figures (Fig. 7). There was such gross proliferation of these cells that they blocked the lumina of the ducts. It was apparent at this stage that these cells were malignant, and it is thought that these were eventually responsible for the patient's death. It is not surprising that the

metastases were of an adenomatous type if these cells were of gland duct origin.

The condition is therefore analogous to Paget's disease of the nipple with breast carcinoma ; this analogy becomes more close when one recalls that the breast is a modified apocrine gland. This would explain the similarity of some of the secondaries in this case to those derived from carcinoma of the breast.

The clinical appearance of the red velvety plaque had some resemblance to some lesions produced by naevus syringadenomatosus papilliferus ; although these usually occur on the scalp they have been reported on other sites, such as the shoulders and groins. Cases of this type of naevus becoming malignant

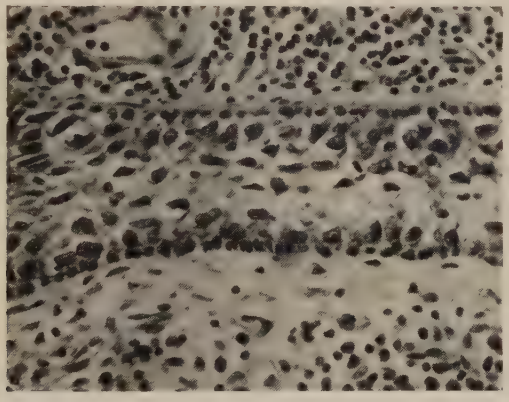

Fig. 7.—Area from main plaque showing a duct lined on its outer surface by small cuboidal cells of the myoepithelial type ; the lumen of the duct is completely filled by large active cells. H. and E. × 200.

have been described by Reuterwall (1933), Horn (1944), Stout and Cooley (1951), Teloh (1955) and Teloh *et al.* (1957). In one of Reuterwall's cases the malignant degeneration was described as being of the basal-cell type.

In the present case, the fourth biopsy showed cells invading the dermis that had some features of a basal-cell carcinoma. However, on close examination these cells were not true basal cells, and resembled much more closely the malignant cells within the ducts (Figs. 8 and 9). A case from our collection of anal Paget's disease with skin secondaries showed cells in the metastatic deposits similar to those in the present case, and these were arranged in the configuration of a basal-cell carcinoma.

It is therefore possible that some cases of naevus syringadenomatosus papilliferus that have been described as becoming malignant by developing basal-cell carcinoma were in fact invasions of the dermis by malignant duct cells showing the general arrangement of a basal-cell cancer.

Other authors (Horn, 1944 ; Stout and Cooley, 1951) have described malig-

nant changes in this naevus, and state that the secondaries have papilliferous outgrowths and in this respect resemble the original tumour. The secondaries from the stomach in the present case had definite papillary formations (Fig. 5);

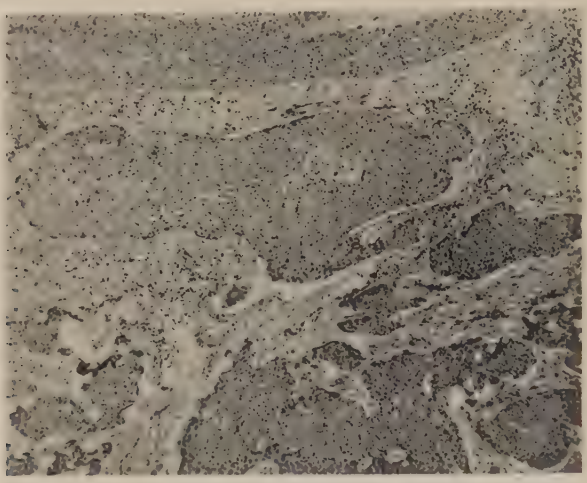

FIG. 8.—Nodule within the main plaque. Invasion of the dermis by duct cells having the general arrangement of a basal-cell carcinoma. The duct in the upper part of the picture contains the same type of cell. H. and E. × 70.

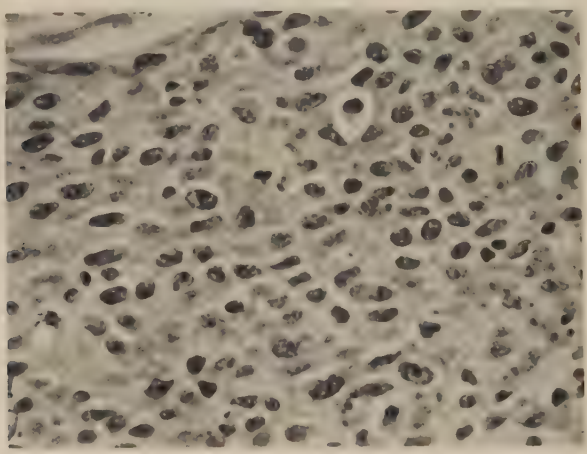

FIG. 9.—Same section as Fig. 7. High power view of the cells invading the dermis, showing mitotic figures and multinucleated cells. These are clearly not basal cells, but are of the same type as those within the ducts. H. and E. × 500.

also the deposits in the thyroid showed two distinct types of cells—some of the myoepithelial type, and some of the larger intra-duct type (Fig. 4).

As some areas of the red granular plaque had the histopathology of Bowen's disease (Figs. 3 and 6), it is possible that *some* cases of this disorder may

be produced by sweat or apocrine duct cell proliferation within the epidermis. Thus some types of "Bowen" or "Paget" cells seen in the epidermis of intra-epidermal carcinomata may be of apocrine or sweat-duct origin. This concept would further strengthen the similarity between the present case and Paget's disease of the nipple.

A review of our collection of intra-epidermal carcinomata revealed two cases in which it appeared that sweat-duct proliferation may have been responsible for the disorder. Also one case of erythroplasia of the penis showed evidence of abnormal changes in the apocrine ducts. Thus it appears possible that some cases of Bowen's disease and some cases of erythroplasia are closely related to Paget's disease in that the epidermis is invaded by malignant cells derived from sweat or apocrine ducts underlying the epidermis.

The present case also suggests a relationship between these disorders and naevus syringadenomatosus papilliferus in which malignant changes supervene in the glandular ducts.

The heavy plasma-cell infiltrate that often occurs in naevus syringadenomatosus papilliferus and erythroplasia, and which was also a marked feature in the present case, may be related to sweat or apocrine duct proliferation. It is possible that when these glandular elements become active and invade surrounding structures, a plasma-cell reaction is excited. Consequently, when these dense infiltrates are seen, a careful examination of serial sections should be made to exclude any pathological changes in the secretory ducts.

Summary.

A case is described of a man who presented with numerous psoriasiform patches of Bowen's disease, and one large brilliant red plaque like erythroplasia.

Histologically, one portion of the erythroplasic patch had the structure of Zoon's type, which he considers non-precancerous, and another portion showed Bowenoid changes in the epidermis. Later, this plaque became frankly malignant and spread rapidly as cancer *en cuirasse*. It also gave rise to copious visceral metastases which proved fatal. Some of these resembled secondaries from a breast cancer.

Renewed histological studies of the erythroplasic plaque revealed, in the earlier biopsies, evidence of sweat-duct proliferation, and, in the later, features resembling naevus syringadenomatosus papilliferus, except that the duct cells had become malignant and filled the lumen. Some of the visceral secondaries showed similar features.

It is suggested that this is a case of sweat-duct carcinoma with features indicating relationship between naevus syringadenomatosus papilliferus, Paget's disease, both types of erythroplasia and some cases of Bowen's disease.

We are grateful to Dr. W. N. Goldsmith for his help and valuable criticism. We thank Mr. L. C. Nickolls of New Scotland Yard for performing the arsenic estimations of the skin, and Mr. Bligh for the photomicrography.

References.

Castel, P. (1936) *Bull. Histol. Tech. micr.*, **13**, 106.
Civatte, A. (1928) *Bull. Ass. franç. Cancer*, **17**, 297.
Darier, J. (1920) *Ann. Derm. Syph., Paris*, **6**, sér. **1**, 49.
Dockerty, M. B. and Pratt, J. H. (1952) *Cancer*, **5**, 1161.
Fournier, A. and Darier, J. (1893) *Ann. Derm. Syph., Paris*, **3** sér. **4**, 613.
Garnier, G. (1957) *Brit. J. Derm.*, **69**, 77.
Garretts, M., for Goldsmith, W. N. (1956) *Ibid.*, **68**, 210.
Grzybowski, M. (1933) *Ann. Derm. Syph.*, Paris, **7**, sér. **4**, 198.
Horn, Jr, R. C. (1944) *Surgery*, **16**, 348.
Kuznitzky, E. and Jacoby, H. (1938) *Arch. Derm. Syph., Chicago*, **38**, 191.
Queyrat, M. (1911) *Bull. Soc. franç. Derm.*, **22**, 378.
Reuterwall, O. (1933) *Acta path. microbiol. scand.*, Supplement 16, 376.
Savatard, L. (1935) *Brit. J. Derm. Syph.*, **47**, 51.
Smith, J. L. S. and Coburn, J. G. (1956) *Brit. J. Derm.*, **68**, 400.
Stout, A. P. and Cooley, S. G. E. (1951) *Cancer*, **4**, 521.
Teloh, H. A. (1955) *Ibid.*, **8**, 1003.
——— Balkin, R. B. and Grier, J. P. (1957) *Arch. Derm. Syph., Chicago*, **76**, 80.
Weiner, H. A. (1937) *Amer. J. Cancer*, **31**, 373.
Zoon, J. J. (1950) *Ned. Tijdschr. Geneesk.*, **94**, 1529.
——— (1952*a*) *Dermatologica, Basel*, **105**, 1.
——— (1952*b*) *Ned. Tijdschr. Geneesk.*, **96**, 2349.

TRAUMATIC CALCINOSIS OF THE SKIN.

I. B. SNEDDON, M.B. Ch.B., F.R.C.P.,
Consultant Dermatologist, Rupert Hallam Department of Dermatology, Sheffield,
AND
R. McL. ARCHIBALD, M.B., Ch.B., D.I.H.,
Medical Officer, North Eastern Division, National Coal Board.

Quite early in one's dermatological career one becomes familiar with the Koebner Phenomenon. Koebner's original description on 3 May 1872 was of the occurrence of psoriasis in skin damaged by the trauma of a pressure sore caused by riding and of horsefly bites, and in a tattoo mark.

We now know that many other conditions can arise in traumatized skin. Lichen planus and warts are perhaps the most commonly seen but erupting eczema and allergic purpura can behave in the same way. Sarcoid granulomata and chronic discoid lupus erythematosus can also be started by trauma but in all these cases the injury merely initiates the pathological process and as far as we know no exogenous agent is responsible for the skin changes. The following cases were unusual in that they appeared to show a Koebner phenomenon but after investigation it was discovered that an exogenous cause was responsible for the lesions.

Case Reports.

Case 1.—In the spring of 1956, a 29-year-old coal-miner was referred to one of us (I.B.S.) because three weeks after his back had been abraded by a slight fall of roof he had developed a most unusual looking but symptomless eruption on the site of the injuries. He had had no treatment for the abrasions, which were no worse than he had sustained on many previous occasions, and he had continued working as a filler at the coal face.

The eruption covered a large area of his back and consisted of many fine white firm papules 2–3 mm. in diameter, some in ring formation and others linear, the majority of the papules having an erythematous flare around them (Fig. 1). The epidermis appeared to be intact over the papules. There was no itching or pain. Most of the lesions were on the exact area where his skin had been abraded, but a few had developed on the posterior axillary fold where he was sure there had been no abrasions. The rest of his skin was normal. He felt in good health and there was nothing else relevant in his history.

Histological examination showed an intact and normal epidermis but with haematoxylin and eosin there was a metachromatic stained zone in the upper half of the dermis. Stained with Von Kossa this gave a markedly positive reaction for phosphates and it appeared fairly conclusively to be calcification in the dermis. Serum electrolytes including calcium and phosphorus were normal. The case was shown to the North of England Dermatological Society as a case of Traumatic Calcinosis ; this diagnosis was accepted but no one had seen one like it.

Case 2.—A few weeks later a similar case was referred to I. B. S.

This was a 21-year-old miner who had two groups of lesions on his left elbow. The eruption had been present for several weeks. Here again, a series of whitish

papules 2 mm. in diameter were arranged in a line 1½ cm. long. He could not remember any particular injury to the elbow but it was reasonable to suppose that he had abraded it.

The histology in this case was not identical with the first since there was a break in the epidermis and the gap was filled with metachromatic staining structureless material which did not stain completely with Von Kossa reagent. However, the two cases were so similar it was concluded that they must be variants of the same pathology.

It was then discovered that these men worked at the same colliery and were at the same part of the coal face. In discussing their working conditions, both patients said that there had been a lot of water dripping from the roof in recent weeks but the conditions were not unusual. A visit to the coal face where the men worked was arranged, as by this time it appeared that there must be some exogenous cause—the series of coincidences admitted no other explanation.

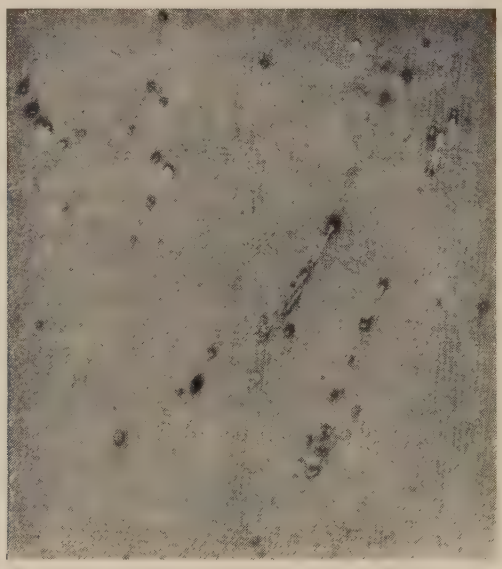

Fig. 1.

After the usual tiring walk for miles underground, we reached the face where these men were employed. Much water was dripping from the roof and it obviously had a very high mineral content, since a glistening white deposit was left on the roof as the water evaporated. In places this was several millimetres thick and could be scraped off. The twelve men who were working in this area were examined ; none showed abnormal skin lesions, though they said that they suffered from irritation when the water soaked their bare backs. Samples of the roof water were analysed by the National Coal Board Scientific Department and contained approximately :

3½% calcium chloride
1% magnesium chloride
10% sodium chloride.

At that time we had been unable to trace any record of similar cases, so in order to confirm the aetiology an attempt was made to produce the lesion experimentally. The skin of the forearm of I. B. S. was scarified with a cutting needle as deeply as pain would allow and a gauze dressing soaked in a solution of the same mineral con-

tent as the roof water was applied. This was kept moist with fresh lotion for 72 hours. At that time obvious calcium deposits appeared in the scratch marks with a considerable inflammatory reaction around them (Fig. 2).

Biopsy was disappointing since it was not possible to demonstrate the calcium deposit which must have fallen out during the handling of the specimen.

The calcium deposits remained clinically visible for six weeks, being gradually extruded. This was a speedier recovery than the coal-miners had, presumably because the abrasions were not so deep. The miners recovered in four months.

Fig. 2.

Discussion

A clue to other work on the subject was given in an article by Zackheim and Pinkus (1957) on calcium chloride necrosis of the skin. They described two cases of calcium deposits in the skin occurring in patients who had handled pure calcium chloride powder, and referred to earlier reports of similar conditions. The first account was in 1935 by Oppenheim. He described papules on the foot and leg in an ice-cream maker who dropped concentrated calcium chloride on his feet, but no histological examination was made. He also produced similar lesions in a rabbit by intracutaneous injection of 10% calcium chloride.

Heppleston in 1946 reported a case which resembles ours closely, even to the

white raised papules, some looking like splashes, in a man who was using a 40% aqueous solution of calcium chloride as a spray to suppress dust in a coal mine. Ulcerated lesions occurred where rubber boots had chafed his legs. Histological examination of the papules showed normal epidermis but necrotic collagen impregnated with calcium in the dermis. Ulcerated lesions have also been reported by Nash (1955) and by Edmonds (1955). The latter described only punched-out ulcers and dermatitis, and found that the roof water of the colliery where there was dermatitis had a content of:

5% calcium chloride
1% magnesium chloride
12% sodium chloride.

This closely resembles the roof water in our pit.

It appears, therefore, that calcium chloride can produce necrosis of the collagen followed by calcinosis. This can occur even through intact skin, and the calcium chloride need be only dilute since in the roof water $3\frac{1}{2}\%$ was sufficient concentration to produce the change. Although this condition is obviously a rare one, it is an interesting phenomenon and might have some application in the study of the formation of renal calculi. It has usually been suggested that some organic nucleus is required to form a renal calculus but deposition of salts might occur beneath the mucosa of the pelvis of the kidney and be later extruded.

Summary.

Two cases of calcification of the skin in coal-miners are described. The cause was identified as the roof water of the coal-mine which contained $3\frac{1}{2}\%$ of calcium chloride. The lesion was reproduced experimentally by applying a similar solution to the scarified skin.

Other examples have been previously reported but much higher concentrations of calcium chloride were responsible.

References.

Edmonds, O. P. (1955) *Brit. J. industr. Med.*, **12**, 320.
Heppleston, A. G. (1946) *Ibid.*, **3**, 253.
Nash, P. H. (1955) *Brit. med. J.*, i, 586.
Oppenheim, M. (1935) *Wien. klin. Wschr.*, **48**, 207.
Zackheim, H. S. and Pinkus, H. (1957). *Arch. Derm., Chicago*, **76**, 244.

ANTIBIOTICS AND SKIN TUBERCULOSIS.

Professor CLAUDE HURIEZ and Dr. P. H. PELCE.

Dermatological Department, Lille University.

This account is based on statistics of our own department, relating to 400 cases treated in Lille between 1941 and 1957. So large a number is due to the fact that the North of France is still the area in which tuberculosis is most common. Its climate is cold. Moreover it is the most industrialized area in the country, containing 200,000 miners out of three million inhabitants. In 16 years we have observed 211 cases of lupus, 9 primaries, 40 verrucous, 43 ulcero-gummatous, 64 scrofulodermas, and 33 tuberculides.

The poor results of local treatment were completely transformed after 1943, when we began to use high doses of vitamin D_2. This brought about very impressive recoveries especially in some advanced cases of lupus, either "exedens" or "tumidus". But after such time as is required for proper perspective, we could record only one-third of complete cures, one-third of improvements, and one-third of failures. The results in other varieties of skin tuberculosis were even less favourable.

The first antibiotics, so far as they were limited to treatments of two or three months, did not seem to give better results in lupus than calciferol; but in the more inflammatory forms of tuberculosis such as verrucous, gummatous and ulcero-vegetant, streptomycin or PAS were more promising.

At the Tenth International Congress of Dermatology in 1952 we suggested a formula associating antibiotics as a medication against the bacillus, with large doses of vitamin D_2 whose sclerosing action we mentioned at this time ; this was before undertaking our researches on animals, which were going to prove its cortisone-like effect.

Isoniazid improved the results to such an extent that many dermatologists thought that it was able by itself to cure all skin tuberculosis. Indeed, isoniazid can bring about cures of very old lupus of 20 or 40 years' duration, of resistant lesions such as some cases of verrucous lupus on the limbs, or prominent "lupus tumidus". Treatments lasting 12, 18, 24 months are required.

Yet, this mono-antibiosis sometimes happens to fail, especially in cases of localized lupus, or lupuses with small disseminated elements. In those cases streptomycin and intravenous PAS must be given as well.

We now reckon 68% of cures in lupus.

Primary lesions resistant to calciferol have often yielded to antibiotics. Injections of izoniazid into lymph glands are combined with systemic antibiotics and followed by long treatments with vitamin D_2. This method brings about 80% recoveries. Yet this form of cutaneous invasion of tuberculosis is not

always harmless on account of its power of lymphatic extension which is still sometimes fatal.

In verrucous lesions isoniazid brings about remarkable recoveries.

Among mucous membrane lesions we have obtained very good results in one case of palatal tuberculosis, following a lip lupus, but without any pulmonary lesion in the past. A child was also cured of lip tuberculosis, though the regional glands were long to disappear.

In the same way we have been able to cure some cases with gummatous lesions of the legs.

In France, scrofuloderma is not observed any more, except among some North African workers who have come to live in the North of France where the climate is too severe for them. Of these only 15% recover with vitamin D_2, 75% with streptomycin or PAS and calciferol, and 55% with isoniazid alone; this reaches 80% if steroids, locally or systemically, are added to the treatment.

In the treatment of tuberculides such as Bazin's disease, injection of large doses of vitamin C remains essential.

In the last five observations of sarcoidosis the combination of antibiotics with steroid removed the angio-lupoides and hypodermic sarcoids without altering pulmonary lesions.

Such are the results of the last five years' therapeutic policy. Recoveries reach 100% in verrucous and ulcero-vegetant forms; they are 80% in the primaries and scrofuloderma, and 68% in lupus vulgaris.

Still some conditions must be absolutely fulfilled; we must

(i) keep on using antibiotics for one year at least;

(ii) associate streptomycin over three to six months with isoniazid;

(iii) add intravenous PAS to the combined isoniazid and streptomycin if necessary;

(iv) always complete the action of antibiotics with intensive and prolonged calciferol;

(v) reserve the association of steroids with antibiotics at present to such uncommon cases as resist isoniazid and calciferol.

Marchionini, de Graciansky, and especially Vandermeiren and Achten, by means of repeated biopsies, have traced the stages of recovery :

(i) After 15 to 30 days, an increase of the number and size of the giant cells, the nuclei of which multiply, probably in connection with the disintegration of tubercle bacilli.

(ii) A second phase is characterized by the transformation of typical tuberculosis follicles into lymphoid follicles.

(iii) Finally comes the phase of repair. New reticulin fibres appear and a collagenous sclerosis leads to complete healing.

Vitamin D_2 causes some proliferation of young connective-tissue fibres which pass between the tuberculous follicles, forming an annular sclerosis something

like the cirrhotic process in the liver. This process can sometimes be seen with the naked eye, the lupus follicles being reduced to small islands.

Later, I have shown with my colleague Professor Tuchmann that large doses of calciferol have cortisone-like properties. In experiments carried out on 600 mice we have determined that the administration of calciferol produces hypertrophy of the zona fasciculata of the suprarenal, indicating hyperactivity. Small doses give rise to cortical hypertrophy and larger doses to marked vascular congestion. We conclude from this that calciferol brings about a non-specific response in the pituitary-suprarenal system.

We have studied the influence of vitamin D_2 on isoniazid metabolism; the free form was titrated by Morse and Curry's biological method, and the total form by Mr. Baelden who used Rubin's chemical method.

Calciferol brings about nearly always an appreciable rise of isoniazid concentration in the blood which is further increased if cortisone is given as well.

This may be an explanation of the potentializing effect of the steroids which has enabled us to cure the few cases of lupus which prove resistant to antibiotics alone. In these cases local injection of hydrocortisone is also useful for its anti-inflammatory effect.

In short, intensive calciferol therapy has been adequate by itself in a proportion unknown until 1943. But in those cases where bacilli are rather scarce and not very virulent, prolonged antibiotics are required to obtain permanent recovery.

Antibiotics are adequate by themselves to cure tuberculosis other than lupus with inflammatory lesions and virulent bacilli, but even so the addition of large doses of calciferol is rather useful to strengthen the recovery. All forms of skin tuberculosis ought therefore to be treated by this calciferol-antibiotic therapy and only in case of need by the addition of steroids. This follows a general tendency in the treatment of infections to associate a specific antibacterial medication with a non-specific agent.

Common sense advises us to take advantage of all attainments of the present time, and yet not to neglect those of the recent past, which succeeded for their part in altering the prognosis of skin tuberculosis, a disease which is now doomed to disappear.

SKIN COLOURING IN RODENT ULCER WITH SPECIAL REFERENCE TO JUTE-WORKERS.

OWEN A. FINN, M.D.

Senior Registrar, Department of Dermatology,
University of St. Andrews, and Royal Infirmary, Dundee.

In 1927 Molesworth emphasized the importance of the action of sunlight, especially on a fair skin, in the production of rodent ulcer. The influence of prolonged exposure to sunlight on different types of skin is now well known ; the blond blue-eyed person is much more prone to skin carcinomata than the darker-skinned individual. Kinnear and his colleagues (1954) observed that jute workers with rodent ulcer did not follow this general trend and suggested that although sunlight is a factor in producing rodent ulcers in general, it has little to do with their appearance in jute-workers. At that time the figures for rodent ulcers were too small to be used statistically and the purpose of this paper is to correct this statement by presenting the findings in 236 consecutive patients with rodent ulcers. In the majority of cases the diagnosis was based on clinical examination but where there was any doubt it was confirmed histologically.

The patients were classified as " fair " (blue, grey, green or hazel eyes with any colour of hair) and " dark " (those with brown eyes). Of the 236 patients, 208 (88·1%) were classed as " fair " as compared with 64·5% " fair " in a control group of 640 patients who showed no malignant change. The control group was the same as that used by Kinnear *et al.* (1954) in which no significant difference was found between the percentages of fair persons in jute-workers and in non-jute-workers. In the present study the patients with rodent ulcers were divided into " jute-workers " (i.e. anyone who had at any time worked in the jute industry), and " non-jute-workers ". Table I shows the sex incidence and percentage of " fair " and " dark ".

TABLE I.

Total	Jute-workers = 74.		Non-jute-workers = 162.	
	Fair	Dark	Fair	Dark
Males, 115	17	3	86	9
Females, 121	46	8	59	8
236	63 (85·1%)	11 (14·9%)	145 (89·5%)	17 (10·5%)

From Table I it will be seen that in 74 jute-workers 85·1% were " fair " and of 162 non-jute-workers, 89·5% were regarded as " fair ". This difference between jute-workers and non-jute-workers is not significant ($\chi^2 = 0{\cdot}45$). Thus, the incidence of rodent ulcer in jute-workers agrees with the generally

accepted belief that basal-cell carcinoma occurs predominantly in fair-skinned individuals.

In 1955 Kinnear *et al.* showed that premalignant and malignant changes occur more often in spinners than in workers in other departments and suggested that these changes might be due to contamination by oil thrown off in minute droplets either from the prepared jute fibre or from the machinery. In the present study of 74 jute-worker patients with rodent ulcer, 18 (24·3%) were spinners and 16 (21·6%) weavers; the remaining patients worked in the other departments of the industry (batching, preparing, winding, dressing, calender, sewing, etc.). The proportions of "fair" amongst the workers in all departments did not differ appreciably from each other ($\chi^2 = 1{\cdot}7$ with two degrees of freedom). The 1951 census of all jute-workers in Scotland shows 4112 (21·5%) weavers and 2113 (11·1%) spinners out of a total of 19,085 workers. Assuming that the census figures are applicable to this survey, this indicates that the incidence of rodent ulcer in weavers is normal but that in spinners it is high ($\chi^2 = 12{\cdot}68$ with two degrees of freedom). This suggests that a factor other than complexion is involved and I believe that, in spinners, mineral oil is the carcinogen which stimulates the arrested embryonal "primary epithelial germ cells" (Lever, 1948) to produce rodent ulcers.

Summary.

Two hundred and thirty-six patients with rodent ulcer are classified according to eye colouring and 88% were found to be "fair". In 74 jute-worker patients with rodent ulcer, 85% were "fair".

The incidence of rodent ulcer in spinners is particularly high and this is presumably related to the carcinogenic effect of mineral oil.

I wish to thank Dr. J. Kinnear and Dr. J. Rogers for permission to use their cases and for their helpful advice. I am indebted to Dr. W. A. Wilson, Lecturer in Public Health, Queen's College, Dundee for assistance in the statistical appraisal.

References.

Kinnear, J., Rogers, J., Finn, O. A. and Mair, A. (1954) *Brit. J. Derm.*, **66**, 344.
——— ——— ——— ——— (1955) *Brit. J. ind. med.*, **12**, 36.
Lever, W. F. (1948) *Arch. Derm. Syph., Chicago*, **57**, 679.
Molesworth, E. H. (1927) *Med. J. Austral.*, i, 878.

ROYAL SOCIETY OF MEDICINE

SECTION OF DERMATOLOGY.

President—Dr. Douis Forman.

20 June 1957.

Folliculitis Ulerythematosa Reticulata (Atrophodermia Vermicularis).—Dr. S. C. Gold.

A woman aged 21 complains of a progressive "pocking" of her cheeks. This process started at the age of six and has recently tended to spread. There has been no inflammatory episode nor has there been any acne of consequence. The changes are confined to the cheeks and they are symptomless.

The family history is negative.

On examination.—There is a reticulated pattern spreading over the cheeks symmetrically down towards the angle of the jaw and forward to the zygoma. There are many small atrophic areas separated from each other by a network of ridges producing a honey-comb appearance. The individual pits vary in size from one to three millimetres across and they have sharp, perpendicular walls. The pits vary in shape as well as size while the ridges, which are on a level with the surrounding normal skin, feel harder by comparison. The pits appear erythematous. There are a few comedones but no milia.

Purpura Annularis Telangiectodes.—Dr. D. C. G. Bett for Dr. Brian Russell.

A woman aged 34. Six months' history of brownish-red oval areas on thighs and buttocks, spreading out to form ringed lesions. The lesions show fine purpuric spots, and some scaling. They do not itch. There is no history of any previous skin trouble, and she has been taking no drugs.

Investigations.—Hess's test was negative.

R.B.C's. 3,000,000/cu.mm., Hb. 66%, total W.B.C's. 5800/cu.mm., differential count normal, bleeding time 2 minutes 50 seconds, clotting time 4 minutes 30 seconds, E.S.R. 8 mm./1 hour, W.R. and Kahn negative.

A biopsy was taken but the histology was reported as "not diagnostic" (Dr. H. Haber).

Postscript.—The lesions have since cleared, leaving no scar.

Histiocytoma.—Dr. P. J. Hare.

A man, aged 52, a librarian.

History.—This man has a long history of sinusitis, for which he had Caldwell-Luc antrostomies performed in 1940. Extensive submucous resection resulted in atrophic rhinitis from which he still suffers. He has also a history of prolonged diarrhoea, lassitude and depression which improved under psychiatric treatment. No pain in the chest or legs. No relevant family history.

The skin lesions began in 1944 with pea-sized, hard nodules on the palmar surface of the left hand and thumb and the right second finger. One of them was removed surgically at another hospital and according to the patient was reported to resemble a neurofibroma. Another lesion he was advised to burn out with nitric acid, which he did, causing considerable pain; this has left only a slight scar.

Since then, the nodules have increased in number and some have grown so large that he cannot lie comfortably in bed.

On examination.—He is generally fit. The blood pressure is 150/90, the peripheral pulses are easily felt and the vessels are soft. On the chest there are several seborrhoeic

warts, some moles and numerous Campbell de Morgan spots. There is erythrasma in the groins.

There are 12 nodular dermal lesions or scars where they have been removed. Pea-sized, skin-coloured or light brown nodules are present on the thighs, right shoulder and the flexor aspect of the left thumb. Flat, button-like indurations, 1·5 cm. in diameter, are present on the lateral surface of the left arm near the elbow and on the sides of the chest. On the right side of the back and on the front of the left thigh there are two hard lesions about 3·5 cm. in diameter, the centres of which are protuberant, purplish-brown and in places yellowish. The lesions are not tender on pressure.

Investigations.—Plasma cholesterol 231 mg./100 ml. X-rays of bones (skull, pelvis, chest and long bones examined) : normal.

Histology.—A button-like lesion shows elongated rete ridges overlying a substantially normal papillary body. In the mid-dermis there is an elliptical nodule composed of fibroblasts and histiocytes with a pale-staining fibrous stroma. These elements form bands and whorls. Centrally, there are accumulations of foam cells. No Touton giant cells are present, but there are a few small multinucleate cells. Fat stains reveal lipoid, not only in the obviously foamy cells, but throughout most of the lesion. Polarized light shows particulate birefringence but no Maltese Cross patterns. Ferric iron is only faintly detectable.

Comments.—This case is shown because of the presence of numerous lesions some of which look clinically almost like xanthomas. Others are or have been present on the fingers, either in the flexor creases or in apparent relation to flexor tendons. Lipidization is shown unusually well ; in contrast remarkably little iron is present.

Postscript.—Some of the lesions were removed under a general anaesthetic. The day after the operation, the patient died and on post-mortem examination he was found to have an extensive dissecting aneurysm of the aorta which had ruptured into the peritoneal cavity. The coronary arteries and aorta showed only moderate atheroma.

Arterio-venous Aneurysm of Right Arm.—Dr. K. M. Witham for Dr. A. Jarrett.

A woman aged 60 years, complaining of (1) swelling in front of right wrist for 27 years, (2) pain in hands for about 10 years, now only on right, (3) swelling of dorsum of right hand for about 2 years and (4) painful right shoulder for 3 years.

History relevant to above.—Said to have been treated for " T.B. of bones of right forearm " as a child.

1932—Ganglion removed from dorsum of right wrist and again in 1939.

1940—Colles fracture right wrist.

1943—Surgical exploration of swelling at front of right wrist which had been present for 14 years and clinically was thought to be tuberculous tenosynovitis. No abnormality was found apart from hypertrophy of flexor digitorum sublimis.

1945—Swelling again explored at another hospital and hypertrophy of the flexor to the index finger was noted. The dorsum of the hand remained swollen for some time after this operation.

1947—Developed pain in fingers which became blue and cold in attacks.

1951—There was swelling of the proximal interphalangeal joint of right middle finger, eventual subsiding.

1954—Developed pain and swelling of right hand and during the winter the skin " cracked " and took a long time to heal over the dorsum of the hand.

1955—Swelling occurred in the upper third of the forearm and again in the cold weather the skin " split " and healed very slowly.

On examination.—Nothing abnormal on general examination apart from some painful limitation of movement of the right shoulder and wrist.

There is an oedematous swelling of the right forearm, dorsum of hand, and front

of the wrist. Discoloration of the right hand which is sometimes pink and hot, but at other times blue and cold.

Investigations.—Skiagrams of hands, shoulders, cervical spine, and chest revealed no abnormalities. E.S.R. repeatedly normal, W.R. negative, biopsy of dorsum of hand showed no histological abnormality apart from oedematous collagen.

Infra-red photography of the hand and forearm failed to demonstrate any abnormal vessels. Radio-sodium blood-flow studies did not show any difference between the skin flow rates of the two hands despite a difference in temperature of 3° C. (the right hand was the warmer). Skin flows at maximum dilation also failed to show any differences. Arterial angiography showed collections of abnormal vessels and there was a suggestion of an arterio-venous shunt in association with the radial artery.

Plethysmography kindly undertaken by Dr. Harold Lambert showed evidence of gross changes in the rate of blood flow in the affected hand and arm.

Right arm : 18·7 ml./100 ml. arm/min.

Left arm : 5·3 ml./100 ml. arm/min. (within normal limits).

These findings are strong evidence of a large arterio-venous shunt in the tissues of the right forearm.

Exploration of the right forearm was performed by Mr. D. Bailey on 18.iii.57. Several abnormal collections of vessels were found and ligated, but no arterio-venous aneurysm was located. No clinical improvement resulted from the operation ; this may have been due to the fact that no shunt was found. However it was not thought advisable to undertake another surgical procedure until the outcome of the last had been completely evaluated.

Further plethysmographic studies on 9.v.57 showed no alteration of the abnormal blood flow.

The patient has been fitted with an elastic glove for the forearm. No further operative measures are contemplated in the immediate future ; if the clinical state deteriorates further, another exploratory operation would be advised.

The following cases have been published in *Proc. R. Soc. Med.*, **50**, 1021 :

Macular Atrophy of the Skin.—Dr. R. G. Howell.

Ehlers-Danlos Syndrome.—Dr. E. Wilson-Jones (for Dr. H. J. Wallace).

Ehlers-Danlos Syndrome with Spondylolisthesis and Malformation of the Terminal Digits.—Dr. L. Forman.

The following cases also were shown :

Poikiloderma with Mycosis Fungoides.—Dr. Brian Russell.

Parapsoriasis Variegata.—Dr. A. Scott (for Dr. P. Borrie).

Dermatomyositis of One Arm.—Dr. I. Martin-Scott.

Acne Necrotica with Alopecia Universalis.—Dr. Bethel Solomons.

Darier's Disease.—Dr. L. Forman and Dr. A. Porter.

Benign Mucous Membrane Pemphigoid.—Dr. L. Forman.

NORTH OF ENGLAND DERMATOLOGICAL SOCIETY.

Manchester, October 1957.

Case for Diagnosis (? Tuberculosis.) Dr. D. A. Duthie.

History.—A man aged 40. Miner 1932–37. Army service in India 1937–40, Middle East and Europe 1940–45.

First seen in May 1955 with infiltrated erythematous plaques some 3 in. in diameter on the left buttock and outer aspect of the right knee, also a smaller lesion on the front of the right thigh, of about four months' duration.

Investigations.—Hb, W.B.C. and differential, E.S.R. and plasma proteins, all normal. W.R. and Kahn negative. Mantoux 1 : 10,000, 1 : 1000 negative, 1 : 100 positive.

Chest X-ray.—Diffuse opacity lung fields, possibly dust reticulation. No glandular enlargement.

Histology of skin lesion.—Numerous tuberculoid lesions with epithelioid cells and giant cells in the deeper part of the section. Beneath the epidermis there is a heavy diffuse cellular infiltrate. Lymphocytes and histiocytes predominate but there are a fair number of plasma cells, a few eosinophils and scattered multinucleate giant cells. The deeper lesions are indistinguishable from sarcoid.

Progress.—Treatment with streptomycin and INAH, calciferol and cortisone, produced no benefit. Since December 1955 there has been recurrent ulceration of the plaque on the right knee and to a lesser extent on the buttock. The patient has been seen by Dr. R. G. Cochrane who considers that the condition is not tuberculoid leprosy.

Postscript.—March 1958. The patient was treated with oral Sterogyl 600,000 units once a week as suggested by Dr. Ingram. This was stopped after 10 doses owing to an increase in the area of ulceration. Following ten weeks on streptomycin, P.A.S. and INAH, the ulceration has almost healed and the plaques are starting to resolve.

Poikiloderma (? Dermatomyositis.) Dr. E. M. Donaldson.

A Polish housewife, aged 58.

History.—Referred in July 1953 with three months' history of itching and redness on backs of fingers and hands, spreading to the forearms and " V " area of neck. The eruption on the forearms and neck showed lichenoid papules on an erythematous base and streaky erythema over the backs of the fingers and hands. Her general health was good except for diabetes mellitus. No muscle weakness.

During the following two years, she developed uniform erythema of forehead and cheeks, areas of reticulate erythema, telangiectasis and atrophy on the sides of neck, trunk and abdomen, and vascular dilatation of the finger-nail folds.

She has had no treatment except indifferent control of diabetes with insulin.

Investigations.—Blood normal, including proteins, E.S.R. and W.R. No L.E. cells seen. Bone marrow normal. Skin histology shows loss of rete pegs with some hyperkeratosis, patchy liquefaction degeneration of the basal cells, and fibrinoid degeneration of the upper dermis with some infiltration of histiocytes and lymphocytes. The appearances are consistent with poikiloderma.

Comment.—At a meeting of the British Association of Dermatology in 1955, it was suggested that her skin lesions were poikilodermatous and probably an expression of internal malignant disease. These lesions have now remained unchanged for two years and her general health is good. Systematic investigation with special reference to visceral malignant disease and reticuloses is negative.

This case would seem comparable with those shown by Vickers and Sneddon at the Royal Society of Medicine in 1955.

References.

Vickers, H. R. (1955) *Brit. J. Derm.*, **67**, 20.
Sneddon, I. B. (1955) *Ibid.*, **67**, 21.

Calcinosis Universalis.—Dr. R. H. Seville.

A girl aged 13.

History.—Nodules on the right knee and the left elbow for $2\frac{1}{2}$ years and on the right fourth toe for 2 years, otherwise perfectly fit. The right toe became painful 18 months ago and discharged some chalky material. It healed after treatment with gentian violet ointment.

The patient has complained of dead fingers in cold weather since she was five. She had a daily teaspoonful of cod liver oil as a baby and more recently a halibut liver oil capsule thrice daily in the winter "as a tonic". There is no evidence of scleroderma or dermatomyositis.

Investigations.—X-rays show amorphous calcification lying in the soft tissue in front of the right knee joint, the tip of the right fourth toe and down the anterior surfaces of both tibiae.

Plasma inorganic phosphorous 4·0 mg.%. Alkaline phosphatase 19 units/100 ml. (The phosphatase is not unduly raised for the patient's age.)

Favus.—Dr. R. H. Seville.

History.—A woman aged 31, who has had trouble with her scalp since she was 8, starting with scaling followed by loss of hair. She was admitted to a hospital in Liverpool when 11 and was an in-patient for 10 months. Her mother says that the patient's hair was removed with x-rays and she was thought to be clear when she was discharged. No abnormality was detected until the hair became thin 7 years ago and 2 years later she developed small patches of baldness. It is only recently that thick yellow crusts appeared which had the characteristic mousy smell. *Trichophyton schoenleini* has been cultured and there is a yellowish-green fluorescence with Wood's light. Her mother's hair is normal and as far as is known, her ancestry is English. She has had asthma for 5 years but the sputum is negative for fungus on microscopy and culture.

Treatment.—The crusts were easily removed with ung. hyd. ammon. aquosum. She was then treated with $\frac{1}{2}$% dithranol in Lassar's paste which produced a normal erythematous reaction and staining and considerable reduction in the number of fluorescent hairs. This treatment has been continued in conjunction with manual epilation at monthly intervals under Wood's light.

Comment.—Although vastly improved, the patient was shown because the relapse took place long after a supposedly successful epilation.

The patient's daughter, aged 4, has had favus of scalp for a year and it is proposed to treat her by x-ray epilation when her mother is clear.

BOOK REVIEWS

A Japanese Atlas.*

If there is a place for atlases in the teaching of dermatology the two volumes under consideration are excellent of their kind.

The pictures are all prints of colour photographs and, whatever the process employed, they are considerably less inaccurate than is usually the case. All the patients portrayed are Japanese and, therefore, the basic colour of the skin in nearly all the examples is slightly more yellow than that usually found in Europeans. Taking this into account the colour values are excellent. Most of the pictures are sharp and the small amount of text accompanying each one is adequate.

The arrangement of the diseases in the two volumes appears to follow no particular plan but it occurs to the reviewer that they may have been arranged alphabetically in Japanese. A number of rare conditions are shown and it is interesting to find illustrated such diseases as acropigmentatio reticularis and Ota's naevus. Plate 49 in the second volume described as Hyperkeratosis Subungualis is almost certainly an example of pachyonychia congenita (Jadassohn–Lewandowski).

Where an atlas is required these volumes are to be recommended. Having said that it is useful to consider how best an atlas may be used for teaching purposes. If placed in the teaching department of a medical school or even in the library it is liable to be rapidly destroyed by hard use. Possibly the most satisfactory is to frame the pictures individually and to hang them labelled and lit in a gallery or passage. J. L. F.

Polymyositis.†

In this most interesting monograph, the authors discuss dermatomyositis and closely related syndromes.

Writing with the experience of 40 personally observed cases, they point out how often the diagnosis is overlooked, particularly in those subacute and chronic cases with minimal skin changes. Fourteen of their 40 cases had been diagnosed as muscular dystrophy and in only 5 of the 40 cases had the correct diagnosis been made in the first place.

The authors use a classification which divides their cases into 4 groups depending on the degree of muscle weakness, the extent of skin changes, the association with other collagen disease or with malignant disease. This grouping, when broken down into tables of age and sex incidence, tends to confuse the reader. The analysis of presenting symptoms underlines how easily polymyositis may be mistaken for a neurological disorder and this chapter is particularly useful to the clinician, be he neurologist, general physician or dermatologist. The following chapter reviews the results of all the investigations including electromyography ; the latter is of value in distinguishing myositis from muscular dystrophy.

The results of treatment with ACTH and cortisone were similar to those of other investigators, some cases showing a favourable response, others none. The clinical findings were no assistance in forecasting which case would respond.

The chapter on pathology contains may beautiful microphotographs of the diverse

---

* *Colour Atlas of Skin Diseases.* 2 Volumes. G. Harada *et al.* (1956). Tokyo : Kanehara Shuppan Co., Ltd. British Agent : London : H. K. Lewis & Co. Ltd. 200 Plates. Price £22.

† *Polymyositis.* John L. Walton and Raymond D. Adams (1957). Edinburgh and London : E. & S. Livingstone Ltd. Pp. 270. 47 Illus. Price 32*s.* 6*d.*

changes which were found in muscle. The importance of choosing for biopsy a muscle weakened by the disease is stressed, as is the focal damage which may exist. No definite pattern of change was found to occur in any clinical group of cases and in many the findings were entirely non-specific.

An appendix contains the full histories of the cases on which the monograph is based and the book is completed with a full bibliography.

Although perhaps primarily of interest to neurologists, this book will be of great value to dermatologists who share with the neurologist the difficulties in diagnosis of this rare but interesting disease. I. B. S.

Civatte's Atlas of Histopathology.*

After his retirement Civatte set himself the task of re-examining and re-assessing his large collection of histological sections accumulated over a period of fifty years. He planned to write, not a comprehensive text-book of cutaneous histopathology for which he would have had to draw largely on the published observations of others, but an atlas recording his personal observations and based exclusively on his own material, with emphasis on the commoner skin disorders. He died before this work was completed. The present volume contains the chapters which would have formed the first of a series of monographs and have been revised and prepared for the press by Dr. Jean Civatte, the author's son.

In his introduction Civatte modestly discusses the limitations of conventional histopathology; the future lies with the histochemist. Simple morphological histology still has its value as a research tool and few clinicians would willingly dispense with its assistance in clinical diagnosis. This remarkable book presents detailed and superbly illustrated accounts of the histopathology of eczema, seborrhoeic dermatitis, senile and seborrhoeic keratoses, psoriasis, lupus erythematosus, lichen planus, lichen sclerosus and parapsoriasis. The early stages, the unusual forms, the atypical variants are described and illustrated, their interrelations are discussed and diagnostic criteria are defined. The cases submitted to biopsy are so often atypical that both to the clinician and to the general pathologist, who ventures only rarely and perhaps unwillingly into the Lilliputian jungles of skin pathology, this book should prove invaluable. If the conclusions on pathogenesis which Civatte draws from his observations are not always universally accepted, nothing can reduce the value of the observations themselves, recorded with scrupulous and meticulous care.

The illustrations, 211 in number, consist mainly of drawings which are effective and illuminating. There are a few photomicrographs, one or two of which are less satisfactory. The quality of the illustrations as a whole is such that the book can be strongly recommended even to those whose knowledge of French is rudimentary. Civatte's prose is, as always, concise and lucid and a pleasure to read. The book is well produced and maintains the high standard one has come to expect from Masson.

A. J. R.

Diseases of the Mouth and Lips.†

This is a standard work in the classical tradition, and the author (Professor of Dermatology at the University of Würzburg) has devoted an immense amount of care and industry to a compilation of the accepted facts and debatable theories on this important subject.

**Atlas d'Histopathologie Cutanée.* A. Civatte (1957). Paris: Masson et Cie. Pp. 254. Illus. 211. Price Fr. 8500 (£7 10*s.* 0*d.* approx.).

† *Krankheiten der Mundschleimhaut und der Lippen.* Hans Schuermann (1958). Berlin: Urban and Schwarzenberg. Pp. 524. Figs. 301 and 24 in colour. Price: DM. 88.

Few text-books have summarized the contemporary literature so intensively, thereby facilitating and stimulating reference to original papers.

There are some 300 half-tone clinical and histological illustrations, and 16 colour reproductions from the living subject, in the 503 pages of the concise and expressive text. Great emphasis is laid on differential diagnosis and on the study of microscopical sections in doubtful cases.

Therapeutic suggestions are unusually brief and are limited to such as are specifically proven and accepted in the general experience.

The eleven pages of " Contents " seemingly comprise all the buccal and lip manifestations of dermatopathology, and include headings pertaining to general medicine and the specific fevers ; a prolonged search failed to reveal any notable omission.

Although perhaps the majority of lip and mouth diseases are adequately dealt with in the leading text-books on dermatology there is room enough for a work of this kind intended to assist the internist, the general practitioner, the surgeon and the venereologist (not forgetting the student, whose instruction in this field has not, the author claims, kept pace with the progress of teaching in other branches of medicine). Even the dermatologist when confronted with a buccal problem in, for example, a suspected specific fever, or one of the confusing bullous or ulcerative stomatoses, may profit by the illustrations and a perusal of the section allocated under the appropriate reference in the exceptionally comprehensive index.

Such deficiency diseases as affect the mouth are catalogued alphabetically from vitamines A to H. Worthy of note too is the section on perlêche with its various causes and there are some instructive illustrations of the common eczematous and contact reactions in cheilitis. Aphthae and aphthous diseases of the mucous membrane are discussed in considerable detail and there are two useful tables to assist the differential diagnosis.

Benign and malignant tumours, embryological heterotopes, the reticuloses, the melanoses, artefacts and industrial causes in buccal and lip localization are admirably collated and described.

Of particular interest and importance in these days of the over-riding antibiotic predilection in treatment, are warnings of the occasionally baneful affects on the mouth and on the lips and other muco-cutaneous junctions. These are considered together with the older metallic intolerances, e.g. mercury and bismuth. Stomatitis is commonly caused by penicillin and the author indicts the lozenge and the chewing-gum particularly as the vehicle. Streptomycin is said to be even more toxic. When parenteral injections are preferred it should be remembered that procaine, a notorious sensitizer, is not infrequently incorporated in the ampoule. The sulphonamides do not escape criticism either, and the much graver issues of agranulocytosis, aplastic anaemia and thrombocytopenic purpura are fully discussed, more especially as the mouth and pharynx may provide the first indications of impending disaster.

The dermatologist requiring clinical descriptions of the rarer types of buccal or lip lesion, such as are occasionally present in the lipoidoses and xanthelasma, the reticuloses and the blood dyscrasias, will not be disappointed. None of importance have been omitted, and most are illustrated clinically as well as histologically. A characteristic example may be quoted :

In dermatomyositis, according to Schuermann, the mouth, lips and tongue are involved in 20% of all cases. Following a meticulous and comprehensive review of the cutaneous features of the disease, he goes on to describe in detail the associated buccal, gingival, and lingual abnormalities. These may include (i) erythema of a dull red or bluish tint and oedema, particularly, of the gums and tongue, which may assume a board-like consistency ; (ii) scattered telangiectases on the mucous membranes of the mouth and palate, and on the lips ; (iii) vesicular or bullous reactions leading to very painful erosions, which may involve simultaneously the whole alimentary tract ; (iv) purpura with occasional moderate haemorrhages ; (v) secondary yeast infections ; (vi) varying degrees of xerostomia, leukoplakia and atrophy.

It is clear from his handling of this and many other predominantly cutaneous diseases that the author is an expert dermatologist with years of personal experience in this somewhat neglected field. It could be argued with some justification that this is in fact a text-book of dermatology with a special focus on buccal and lip manifestations. It is certainly well designed, comprehensive, reliable and up to date, and well deserves a place in all medical libraries and on the bookshelves of such dermatologists as are conversant with the German language. H. C. S.

Dermatologic and Allergologic Therapy.*

This is a formidable symposium to review containing as it does over sixty articles mainly by French authors, on subjects ranging from penicillin to plastic planing, and from cortisone to cobalt chloride for psoriasis. The book is divided into five sections :

1. *Antimitotic therapy* includes articles on radiotherapy, podophyllin-colchicine mixtures, nitrogen mustards etc.

2. *Neurotropic therapy* deals with psychotherapy, tranquillisers, and cholinergic urticaria.

3. *Anti-inflammatory and anti-allergic therapy* includes steroids, Nivaquin, heparin, etc.

4. *Anti-infectious therapy* is mostly about antibiotics.

5. *New orientations in therapy* gives scope for a wide range of novelties. The Anglo-Saxon reader is apt to be rather sceptical of clinical impressions based on small series of cases without controls—thus three cases of psoriasis are reported to have improved with a placental extract, and one case of ichthyosis with a vitamin treatment. Nevertheless, one appreciates the brilliant flash of Gallic intuition; antihistamines came from France, and there may be some experiment of permanent value here. Is it for instance true that Nivaquin has an action on a wide range of vascular processes and will cure " nodular vasculitis "? This may well be so but proof will require more than the three cases reported by Bureau and Barriere. The critical reader will find many stimulating ideas here. He will also meet many unfamiliar terms such as orthodermic, anadermic, diadermic and microergic ; whether these neologisms clarify or mystify is debatable. The book opens with a scholarly and philosophical introduction by Charpy and we cannot close this review better than by quoting his words " The evolution of modern therapy is both wonderful and disquieting." F. F. H.

Encyclopedie Medico-Chirurgicale.†

This issue has major articles on diseases due to acari, those due to lesions of the nervous system and sclero-atrophic diseases. As we have come to expect from previous volumes the articles are up to date and based on a careful survey of the world literature, whilst the black and white illustrations are excellent. Among those lesions included in the second group are some that are not strictly nervous in origin such as bed sores, but this chapter is useful in dealing with several conditions in the borderland between dermatology and neurology which are often neglected in dermatological text-books. In dealing very fully with scleroderma, Touraine refers to acrosclerosis but does not seem to regard this as a separate entity from generalized scleroderma. Shorter articles cover among other things cryoglobulins, hyperglobulinaemic purpura, incontinentia pigmenti, acrogeria and Miescher's chronic progressive disciform granuloma. F. F. H.

---

* *Dermatologic and Allergologic Therapy.* Published under the direction of J. Charpy (1957). Paris : Masson & Cie. Pp. 380.

† *Encyclopedie Medico-Chirurgicale.* Edited by A. Touraine (1957), 33rd Section.

Calciferol Treatment of Chromomycosis.*

It is unlikely that many of our readers will see this disease, so for them the interest of this book will be in the method of treating an obstinate granulomatous fungous infection. In addition to the usual iodides, the author also gave calciferol to his 20 patients and followed histologically the sequence of events. First there was an increased histiocytic reaction and the formation of tuberculoid structures, and the cellular infiltration and micro-abscesses diminished. Histological cure, which was later than clinical cure, was represented by the disappearance of the sarcoid-like nodules, substituted by diffuse fibrosis, absence of any residue of infiltration, with the dermis reassuming a normal appearance, and the epidermis becoming fine and flat.

Calciferol was best tolerated in weekly doses of 600,000 units. There is a summary in English.

This method may have possibilities in other chronic granulomatous conditions.

G. W. B.

---

* *Tratamento da Chromoblastomycose pelo Calciferol.* Clovis Bopp (1957). Of. Gràf. da Livraria do Globo. S.A. Porto Alegre. Pp. 183. Fig. 117.

CURRENT LITERATURE

REMITTENT NECROTIZING ACROCYANOSIS. E. A. Edwards. (1956) *J. Amer. med. Ass.*, **161**, 1530.

Twenty cases of a distinctive but poorly recognized type of acral ischaemia have been studied. Hutchinson, Raynaud and Lewis were all familiar with the condition, which probably affects the sexes equally and usually first appears between the ages of 50 and 80. The attacks of symmetrical coldness, cyanosis and pain in hands or feet may begin at any season, may last some months, regress spontaneously and may recur. Necrosis of the tips of fingers or toes may take place. Biopsy has shown perivascular inflammation and endothelial proliferation of arterioles and small arteries of the skin. Some organic obstruction must accompany the vasospasm. The aetiology is unknown. Great care has been taken to exclude the known peripheral vascular syndromes. Treatment has to be restricted to rest, sedation and vasodilator drugs as sympathectomy has proved to be of little value. A. J. R.

SELENIUM SULFIDE IN TREATMENT OF PITYRIASIS VERSICOLOR. H. M. Robinson Jr. and S. N. Yaffe. (1956) *J. Amer. med. Ass.*, **162**, 113.

Thirty-two patients with pityriasis versicolor were successfully treated with 1% selenium sulphide in a water-miscible ointment base. There was no recurrence after one year.

A. J. R.

CHLORPROMAZINE IN THE TREATMENT OF PORPHYRIA. J. C. Melby, J. P. Street, and C. J. Watson. (1956) *J. Amer. med. Ass.*, **162**, 174.

Chlorpromazine in a dose of 25 mg. three or four times a day was followed by prompt disappearance of pain and nervous symptoms in 9 cases of acute intermittent porphyria. There was no evidence of a reduced excretion of porphyrins or porphobilinogen as an early effect of this treatment. In two cases *Rauwolfia* alkaloid was of value in maintenance therapy.

A. J. R.

NYSTATIN (MYCOSTATIN) IN THE TREATMENT OF MONILIAL AND NON-MONILIAL VAGINITIS. H. R. Pace and S. I. Schantz. (1956) *J. Amer. med. Ass.*, **162**, 268.

Monilial vaginitis in 59 women, of whom 31 were pregnant, was treated with Nystatin tablets, (100,000 units) inserted in the vagina at night for 7 to 14 days. Negative cultures and clinical improvement were obtained in 58 cases. Ten of the pregnant patients and 4 of the others relapsed after 2 to 5 weeks, but a further course of Nystatin " gave excellent final results " in all cases.

A. J. R.

CHLORAMBUCIL IN TREATMENT OF CHRONIC LYMPHOCYTIC LEUKEMIA AND CERTAIN LYMPHOMAS. J. E. Ultmann and A. Gellhorn. (1956) *J. Amer. med. Ass.*, **162**, 178.

Chlorambucil (CB 1348) is an aromatic nitrogen mustard. The drug is given orally and effective doses were found to be relatively free from side-effects, and rarely to cause bone marrow damage. Satisfactory responses were obtained in patients with chronic lymphocytic leukaemia but the drug was of less value in lymphosarcoma or Hodgkin's disease. A. J. R.

MUCOSAL PEMPHIGOID. Fr. Kogoj, (1955) *Dermatologia*, **6**, 235.

Description of a case with discussion on the literature and aetiology. The low mortality from the disease itself is mentioned (one case out of thirty). The present patient died with bronchopneumonia. Mucosal pemphigoid affects the eyes or mouth from the start, and produces progressively more severe lesions ; these are characterized by a sub-epidermal bulla. It affects all ages and both sexes. The author prefers the name " dermatitis pemphigoides mucocutanea chronica ".

There is nothing particularly new in this article, which gives full references and discusses the cases shown by Carleton, Sneddon, and others. However, it forms a useful addition to our knowledge of the course and post-mortem findings in these cases. D. S. W.

LEPROSY : SIGNIFICANT ADVANCES DURING THE LAST DECADE. R. G. Cochrane. (1956) *Med. Pr.*, **236**, 246.

This most valuable article should be read by all practitioners who may have to treat patients suffering from leprosy. Although the *Myobacterium leprae* does not fulfil Koch's postulates, there is now no doubt that this is the causative organism. The most probable portal of entry is through the skin.

The problems are dealt with under the headings :

(1) How can a general practitioner recognize a case of leprosy ?
(2) Official procedures to be adopted when the diagnosis is made.
(3) Treatment.
(4) Complications in leprosy.
(5) Disposal of the infective case.
(6) Public knowledge and understanding of leprosy.

In dealing with the diagnosis it must be remembered that leprosy is, like syphilis, a great simulator and must always be considered whenever a person from a leprosy area is suffering from a dermatological condition which does not itch, which does not fit into one of the usual disease patterns and which has been present for more than six months. A nasal smear is almost useless in confirming a diagnosis of leprosy. Skin smears using corium tissue juice are much more diagnostic. Treatment and its dangers are given in detail and the author stresses the importance of educating the general public to remove the stigma conveyed still by the word leprosy.

H. R. V.

THE CRYSTALLINE STRUCTURE OF MELANIN. E. Meirowski, (1955) *Dermatologia*, **6**, 255.

A short, concise and useful account of the methods used to study the melanin granule and a description of its crystalline structure as shown by ultra-sonic waves. Much of the work done on this has appeared in technical and radiological journals. D. S. W.

LOCALISED FORMS OF PEMPHIGUS AND PEMPHIGOID. A. Crosti, (1955) *Dermatologia*, **6**, 210.

An illustrated description of varieties of localized pemphigus-like lesions and their differentiation. The Senear-Usher type of pemphigus is particularly likely to remain localized, sometimes for years. The value of cyto-diagnosis is emphasized. D. S. W.

VISCERAL LESIONS IN PEMPHIGUS VULGARIS. J. Charpy, *et al.* (1955) *Dermatologia*, **6**, 201.

Report of a fourth case in which post-mortem findings in a case of pemphigus vulgaris included hyalinization of the vessel walls and collagenous changes in the tissues. There were also degenerative changes, including lysis, of the cells of the peripheral nerve ganglia. The changes in the fourth case follow, in general, the pattern of those discovered in the three previous cases, but their exact significance is not discussed in detail in this article. D. S. W.

ACTION OF SYNTHETIC ANTIMALARIAL DRUGS ON PSORIASIS. T. Cornbleet. (1956) *J. invest. Derm.*, **26**, 435.

Because mepacrin does good in L.E. and in certain other dermatoses aggravated by light it seemed worth while to try if it would make worse maladies, for example psoriasis, ordinarily benefited by exposure to the sun.

In all of 6 subjects receiving a daily dose (for a period that is unspecified but would appear generally to have exceeded 10 days), of 100 mg. quinacrine 250 mg. chloroquine and 200 hydroxychloroquine the psorasis became worse and began to affect the palms. Three to six weeks after the last dose the psoriasis started to improve and continued to clear until the patient had gained an amelioration of his initial state more or less equal to the worsening induced by the drug.

Next time the doses had to be doubled to get the same effect, and therapeutic usefulness is neither claimed nor expected ; but it is nevertheless hoped that the observation may help to interpret the influence of light on psoriasis.

(If this interesting phenomenon turns out to be one that is open to anyone to observe for himself, it must illuminate a wide field of dermatological pathology and provide a fundamental principle of therapeutics.) J. H. T. D.

THE PATHOGENESIS OF MILIA AND BENIGN TUMOURS OF THE SKIN. W. Epstein and A. M. Kligman. (1956) *J. invest. Derm.*, **26**, 1.

Milia (and, by analogy, benign tumours) may arise from any part of the epidermis: spontaneously for example from the external root sheath of vellus hair follicles, from frustrated sebaceous glands isolated by dermabrasion, from the eccrine duct in epidermolysis bullosa and from any part of the epidermis, but especially the external root sheath, in autotransplants. The thesis of pluripotentiality of all epidermal cells, almost regardless of differentiation, is also supported by our knowledge of the hair cycle in mice, reports of regeneration of appendages in rabbits and rumours thereof in man. But the authors regard it as " more than interesting " that similar conclusions should be reached through the " different disciplines " of pathology and physiologic anatomy ! J. H. T.D.

A SEROLOGIC STUDY OF HYPHOMYCETES CAUSING MYCETOMA IN MAN. A Seeliger. (1956) *J. invest. Derm.*, **26**, 81.

An indigenous case of maduromycosis for many years misinterpreted as intractable actinomycosis has been reported from Bonn.

The author collected 23 strains of mycetoma-producing organisms and has studied their serological reactions and those of a variety of familiar pathogenic and non-pathogenic fungi in the rabbit.

The serum of the author's case contained specific agglutinins, precipitins and complement fixing antibodies, and of sera obtained from 10 African patients in the Belgian Congo several at least contained agglutinins.

Skin reactions corresponded with the results of the precipitin tests. Complement fixation reactions could however be obtained in rabbit sera sensitized to other organisms, e.g. *T. rubrum*, *Penicillium notatum* ; the Bonn patient though not demonstrably allergic to it, gave a positive sero-reaction to penicillin. J. H. T. D.

THE CRYSTALLINE STRUCTURE OF MELANIN KERATIN AND COLLAGEN. E. Meirowsky. (1956) *J. invest. Derm.*, **26**, 95.

Evidence is adduced, from x-ray diffraction ultramicroscopic and polariscopic examination of materials after treatment with hydrogen peroxide and ultrasonic vibrations, to support the hypothesis of a crystalline structure of living matter.

" Protomer ", it seems, is " micelle " with the new look. J. H. T. D.

THE INFLUENCE OF OIL-IN-WATER EMULSIONS ON THE HYDRATION OF KERATIN. J. B. Shelmire. (1956) *J. invest. Derm.* **26**, 105.

Starting from the assumption that the traditional application of grease is the answer to atmospheric hardening of keratin, the author finds that 20% mineral oil and 3% cetyl alcohol emulsified in water with 2% lauryl sulphate " gave a preparation slightly above minimum for maintaining full pliability of callus over a 16-hour period " and that the addition of glycerin tragacanth, etc., diminished its effectiveness.

It appears however to be claimed for this mixture that it secures all the conditions required for the well-being of the horny layer, prevents loss of water, supplies it when required, and prevents maceration by sweat or adventitious damp.

J. H. T. D.

RESPONSE OF THE SKIN OF MICE TO METHYL ETHER OF VITAMIN A AND VITAMIN A PALMITATE. A. H. Rademacher and W. Montagna. (1957) *J. invest. Derm.*, **26**, 69.

Only during the resting phase of the hair growth cycle do these compounds (as also cholanthrene) have any important effect. It seems to be merely one of nonspecific irritation, among other changes accelerating the fall of the club hairs, but without influence on regeneration keratinization or –SH metabolism. It would appear some protective influence is withdrawn during the resting phase.

J. H. T. D.

THE EPIDERMAL ECCRINE DUCT. R. K. Winkelmann. (1956) *J. invest. Derm.*, **26**, 169.

Describes methods of separating the sweat duct from the covering epithelium and staining techniques designed to illustrate its anatomical autonomy. J. H. T. D.